

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2006/311600

A. CLASSIFICATION OF SUBJECT MATTER A61K39/395(2006.01)i, A61K9/19(2006.01)i, A61K47/02(2006.01)i, A61K47/10(2006.01)i, A61K47/18(2006.01)i, A61K47/22(2006.01)i, A61K47/26(2006.01)i, A61K47/46(2006.01)i, A61P43/00(2006.01)i, G01N33/15(2006.01)i, According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) A61K39/395(2006.01), A61K9/19(2006.01), A61K47/02(2006.01), A61K47/10(2006.01), A61K47/18(2006.01), A61K47/22(2006.01), A61K47/26(2006.01), A61K47/46(2006.01), A61P43/00(2006.01), G01N33/15(2006.01), Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Jitsuyo Shinan Koho 1922-1996 Jitsuyo Shinan Toroku Koho 1996-2006 Kokai Jitsuyo Shinan Koho 1971-2006 Toroku Jitsuyo Shinan Koho 1994-2006 Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Caplus (STN), EMBASE (STN), MEDLINE (STN), JMEDPlus (JDream2), JST7580 (JDream2), JSTPlus (JDream2)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y A	COCHLOVIUS B., Treatment of human B cell lymphoma xenografts with a CD3 x CD19 diabody and T cells, Journal of immunology, 2000, Vol.165, No.2, pages 888 to 895	1-6, 9, 14-19, 22 10 12, 13, 23, 24, 36-42
Y	WO 2004/019966 A1 (CHUGAI SEIYAKU KABUSHIKI KAISHA), 11 March, 2004 (11.03.04), Full text & EP 1541165 A1 & US 2006/058511 A1	10
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents: “A” document defining the general state of the art which is not considered to be of particular relevance “E” earlier application or patent but published on or after the international filing date “L” document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) “O” document referring to an oral disclosure, use, exhibition or other means “P” document published prior to the international filing date but later than the priority date claimed “T” later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention “X” document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone “Y” document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art “&” document member of the same patent family		
Date of the actual completion of the international search 17 August, 2006 (17.08.06)		Date of mailing of the international search report 29 August, 2006 (29.08.06)
Name and mailing address of the ISA/ Japanese Patent Office		Authorized officer
Facsimile No.		Telephone No.

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	JP 2003-515323 A (OXFORD BIOMEDICA (UK) LTD.), 07 May, 2003 (07.05.03), Claims; Par. No. [0208] & WO 2001/36486 A2 & EP 1242456 A2 & US 2003/083290 A1 & US 2004/131591 A1 & US 2004/265275 A1 & US 2006/014222 A1	10
Y	JP 2002-543822 A (SMITHKLINE BEECHAM CORP., US), 24 December, 2002 (24.12.02), Par. Nos. [0020], [0075] & WO 2000/69462 A1 & EP 1178829 A1	10
P, X	WO 2005/107784 A1 (CHUGAI SEIYAKU KABUSHIKI KAISHA, JP), 17 November, 2005 (17.11.05), Par. No. [0147]; example 1 (Family: none)	1-6, 9, 14-19, 22
A	KIPRIYANOV S.M., Bispecific tandem diabody for tumor therapy with improved antigen binding and pharmacokinetics, Journal of Molecular Biology, 1999, Vol.293, No.1, pages 41 to 56	12, 13, 23, 24, 36-42
A	Voelkel T., Optimized linker sequences for the expression of monomeric and dimeric bispecific single-chain diabodies, Protein Engineering, 2001, Vol.14, No.10, pages 815 to 823	12, 13, 23, 24, 36-42
A	Meng R., The evaluation of recombinant, chimeric, tetravalent antihuman CD22 antibodies, Clinical cancer research, 2004, Vol.10, No.4, pages 1274 to 1281	12, 13, 23, 24, 36-42
A	JAGER M., Folding and Assembly of an Antibody Fv Fragment, a Heterodimer Stabilized by Antigen, Journal of Molecular Biology, 1999, Vol.285, No.5, pages 2005 to 2019	12, 13, 23, 24, 36-42
A	KORN T., Recombinant bispecific antibodies for the targeting of adenoviruses to CEA- expressing tumour cells: a comparative analysis of bacterially expressed single-chain diabody and tandem scFv, Journal of Gene Medicine, 2004, Vol.6, No.6, pages 642 to 651	12, 13, 23, 24, 36-42
A	KIPRIYANOV S.M., Effect of Domain Order on the Activity of Bacterially Produced Bispecific Single-chain Fv Antibodies, Journal of Molecular Biology, 2003, Vol.330, No.1, pages 99 to 111	12, 13, 23, 24, 36-42

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Continuation of A. CLASSIFICATION OF SUBJECT MATTER
(International Patent Classification (IPC))

G01N33/50(2006.01) i

(According to International Patent Classification (IPC) or to both national classification and IPC)

Continuation of B. FIELDS SEARCHED

Minimum documentation searched (International Patent Classification (IPC))

G01N33/50(2006.01)

Minimum documentation searched (classification system followed by classification symbols)

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
(See extra sheet)

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Part of claims 1-6, 10, 12-19, 23, 24 and 36-42, and claims 9 and 22

- Remark on Protest**
- the ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, payment of a protest fee..
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☒ No protest accompanied the payment of additional search fees.

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Continuation of Box No.III of continuation of first sheet(2)

<Concerning unity of invention>

A. Part of claims 1-6, 10, 12-19, 23, 24 and 36-42, and claims 9 and 22 relate to a pharmaceutical composition containing a salt and sc(Fv)2.

B. Part of claims 1-6, 10, 12-19, 23, 24 and 36-42 relates to a pharmaceutical composition containing an aminosugar and sc(Fv)2.

C. Part of claims 1-6, 10, 12-19, 23, 24 and 36-42 relates to a pharmaceutical composition containing a sugar alcohol and sc(Fv)2.

D. Part of claims 1-6, 10, 12-19, 23, 24 and 36-42 relates to a pharmaceutical composition containing an amino acid and sc(Fv)2.

E. Part of claims 1-6, 10, 12-19, 23, 24 and 36-42, and claims 7, 8, 20 and 21 relate to a pharmaceutical composition containing a pH adjuster and sc(Fv)2.

F. Part of claims 12 and 36, and claims 11 and 25 relate to a lyophilized formulation containing sc(Fv)2.

G. Claims 26-35 relate to a method of suppressing isomerization of an active ingredient in a pharmaceutical composition.

H. Claim 43 relates to a screening method for a substance that suppresses an isomerization reaction of sc(Fv)2.

The pharmaceutical composition containing sc(Fv)2 which is a matter common to A and B-F is publicly known as described in, for example, the document (COCHLOVIUS B, Treatment of human B cell lymphoma xenografts with a CD3 x CD19 diabody and T cells, Journal of immunology, 2000, Vol. 165, No. 2, pp. 888-895).

The pharmaceutical composition which is a matter common to A and G is publicly known without referring to documents.

Accordingly, the matter common to these falls into the category of the prior art, therefore, this is not considered as a special technical feature. Further, there is no other common matter which is common to all the claims and considered as a special technical feature.

H is not a method of producing a substance that suppresses an isomerization reaction of sc(Fv)2 such as a salt or an aminosugar, or a method using these substances. Further, there is no suggestion that relating to a specific structure of a compound required for suppressing an isomerization reaction of sc(Fv)2. Accordingly, there is no single general inventive concept between A and H.

Thus, the number of inventions contained in this application is 8.

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

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- US 3773919 A [0063]
- EP 58481 A [0063]
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Non-patent literature cited in the description

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